

SEQUENCE LISTING

Simmons, Laura <120> METHODS FOR PRODUCING HUMANIZED ANTIBODIES AND IMPROVING YIELD OF ANTIBODIES OR ANTIGEN BINDING FRAGMENTS IN CELL CULTURE <130> 11669.120USU1 <140> US 10/764,428 <141> 2004-01-23 <150> US 60/442,484 <151> 2003-01-23 <160> 33 <170> PatentIn version 3.1 <210> 1 <211> 25 <212> PRT <213> Artificial Sequence <220> <223> FR1 SGI <400> 1 Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala 5 10 15 Ser Val Lys Val Ser Cys Lys Ala Ser 20 <210> 2 <211> 25 <212> PRT <213> Artificial Sequence <220> <223> FR1 SGII <400> 2 Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln 5 10 Thr Leu Ser Leu Thr Cys Thr Val Ser 20 <210> 3 <211> 25 <212> PRT <213> Artificial Sequence

<220> <223> FR1 SGIII

3

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser 20 25

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<211> 3300 <212> DNA

<213> Artificial Sequence

<220>

<400>

<223> pxVG11VNERK

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<210> 5

<211> 670

<212> PRT

<213> Artificial Sequence

<220>

<223> The first 214 amino acids are the light chain followed by the heavy chain beginning at position 215 (E).

<400> 5

Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Ser Ala Ser Gln Asp Ile Ser Asn Tyr 20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Val Leu Ile 35 40 45

Tyr Phe Thr Ser Ser Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly 50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Ser Thr Val Pro Trp \$85\$ 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115 120 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala 130 135 140 Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Ile Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Ala Asp Phe Lys Arg Arg Phe Thr Phe Ser Leu Asp Thr Ser Lys Ser Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Lys Tyr Pro His Tyr Tyr Val Asn Glu Arg Lys Ser His Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp

Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp 625 630 635 640

Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His
645 650 655

Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys 660 665 670

<210> 6

<211> 3300

<212> DNA

<213> Artificial Sequence

<220>

<223> pxVG2AP11

<400> 6

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- <210> 7
- <211> 667
- <212> PRT
- <213> Artificial Sequence
- <220>
- <223> Light chain begins at residue 1 (D); Heavy chain begins at residue 215 (E)
- <400> 7
- Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1 5 10 15
- Asp Arg Val Thr Ile Thr Cys Ser Ala Ser Gln Asp Ile Ser Asn Tyr 20 25 30
- Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Val Leu Ile 35 40 45
- Tyr Phe Thr Ser Ser Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly 50 55 60
- Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro 65 70 75 80
- Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Ser Thr Val Pro Trp 85 90 95
- Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala 100 105 110
- Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
 115 120 125
- Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala 130 135 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr Asp Phe Thr His Tyr Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Ala Asp Phe Lys Arg Arg Phe Thr Phe Ser Leu Asp Thr Ser Lys Ser Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Lys Tyr Pro Tyr Tyr Tyr Gly Thr Ser His Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr

Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe

Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly 625 630 635 640

Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr 645 650 655

Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys 660 665

<210> 8

<211> 3300

<212> DNA

<213> Artificial Sequence

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<223> pVKFR1-2

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- <210> 9
- <211> 670
- <212> PRT
- <213> Artificial Sequence

<220>

- <223> Light chain starts at residue 1 (D); Heavy chain starts at
 residue 215 (Q)
- <400> 9

Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Ser Ala Ser Gln Asp Ile Ser Asn Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Val Leu Ile 35 40 45

Tyr Phe Thr Ser Ser Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly 50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro 65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Ser Thr Val Pro Trp 85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala 100 105 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115 120 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala 130 135 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser 165 170 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr 180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser 195 200 205

Phe Asn Arg Gly Glu Cys Gln Val Gln Leu Val Gln Ser Gly Ala Glu 210 215 220

Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly 225 230 235 240

Tyr Thr Phe Thr Asn Tyr Gly Ile Asn Trp Val Arg Gln Ala Pro Gly 245 250 255

Lys Gly Leu Glu Trp Val Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro 260 265 270

Thr Tyr Ala Ala Asp Phe Lys Arg Arg Phe Thr Phe Ser Leu Asp Thr 275 280 285

Ser Lys Ser Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp 290 295 300

Thr Ala Val Tyr Tyr Cys Ala Lys Tyr Pro His Tyr Tyr Val Asn Glu 305 310 315 320

Arg Lys Ser His Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Leu Val 325 330 335

Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala 340 345 350

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu 355 360 365

Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly 370 380

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu 405 410 415

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr 420 425 430

Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr 435 440 445

Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe 450 455 460

Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro 465 470 475 480

Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val
485 490 495

Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr 500 505 510

Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val 515 520 525

Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys 530 535 540

Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser 545 550 555 560

Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro 565 570 575

Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val
580 585 590

Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly 595 600 605

Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp 610 620

Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp

625 630 635 640

Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His 645 650 655

Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys 660 665 670

<210> 10

<211> 3300

<212> DNA

<213> Artificial Sequence

<220>

<223> pVKSGII

<400> 10

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1260 ctcggttgcc gccgggcgtt ttttattgtt gccgacgcgc atctcgaatg aactgtgtgc 1320 gcaggtagaa gctttggaga ttatcgtcac tgcaatgctt cgcaatatgg cgcaaaatga ccaacagcgg ttgattgatc aggtagaggg ggcgctgtac gaggtaaagc ccgatgccag 1380 1440 catteetgae gaegataegg agetgetgeg egattaegta aagaagttat tgaageatee 1500 tegteagtaa aaagttaate tttteaacag etgteataaa gttgteaegg eegagaetta 1560 tagtcgcttt gtttttattt tttaatgtat ttgtaactag tacgcaagtt cacgtaaaaa 1620 gggtatctag aattatgaag aagaatatcg catttcttct tgcatctatg ttcgtttttt ctattgctac aaacgcgtac gctcaggttc agctgcaaga gtctggcccg ggcctggtga 1680 aaccatetea gaetetetee tigaetigta eigittetgg etalaeette accaactatg 1740 1800 gtataaactg ggtccgtcag gccccgggta agggcctgga atgggttgga tggattaaca cctataccgg tgaaccgacc tatgctgcgg atttcaaacg tcgtttcact ttttctttag 1860 1920 acacctccaa aagcacagca tacctgcaga tgaacagcct gcgcgctgag gacactgccg 1980 totattactg tgcaaagtac ccgcactatt atgtgaacga gcggaagagc cactggtatt tegaegtetg gggteaagga accetggtea cegteteete ggeeteeace aagggeeeat 2040 2100 eggtettece cetggeacee tectecaaga geacetetgg gggeacageg geeetggget gcctggtcaa ggactacttc cccgaaccgg tgacggtgtc gtggaactca ggcgccctga 2160 ccagcggcgt gcacacette ccggctgtee tacagteete aggaetetae teceteagea 2220 2280 gegtggtgac tgtgccctct agcagettgg gcacccagac ctacatetgc aacgtgaatc 2340 acaagcccag caacaccaag gtggacaaga aagttgagcc caaatcttgt gacaaaactc acacatgccc accgtgccca gcacctgaac tcctgggggg accgtcagtc ttcctcttcc 2400 2460 ccccaaaacc caaggacacc ctcatgatct cccggacccc tgaggtcaca tgcgtggtgg 2520 tggacgtgag ccacgaagac cctgaggtca agttcaactg gtacgtggac ggcgtggagg tgcataatgc caagacaaag ccgcgggagg agcagtacaa cagcacgtac cgtgtggtca 2580 2640 gcgtcctcac cgtcctgcac caggactggc tgaatggcaa ggagtacaag tgcaaggtct 2700 ccaacaaagc cctcccagcc cccatcgaga aaaccatctc caaagccaaa gggcagcccc 2760 gagaaccaca ggtgtacacc ctgcccccat cccgggaaga gatgaccaag aaccaggtca 2820 gcctgacctg cctggtcaaa ggcttctatc ccagcgacat cgccgtggag tgggagagca atgggcagec ggagaacaac tacaagacca egeeteeegt getggaetee gaeggeteet 2880 tetteeteta cagcaagete accetegaca agagcagete geagcagege aacetettet 2940 catgetcegt gatgeatgag getetgeaca accaetacae geagaagage etetecetgt 3000

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<210> 11

<211> 670

<212> PRT

<213> Artificial Sequence

<220>

<223> Light chain starts at residue 1 (D); Heavy chain starts at residue 215 (Q)

<400> 11

Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Ser Ala Ser Gln Asp Ile Ser Asn Tyr 20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Val Leu Ile 35 40 45

Tyr Phe Thr Ser Ser Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly 50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro 65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Ser Thr Val Pro Trp 85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala 100 105 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115 120 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala 130 135 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln 145 150 155 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Thr Phe Thr Asn Tyr Gly Ile Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Ala Asp Phe Lys Arg Arg Phe Thr Phe Ser Leu Asp Thr Ser Lys Ser Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Lys Tyr Pro His Tyr Tyr Val Asn Glu Arg Lys Ser His Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp

Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp

Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His 645 650 655

Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys 660 665 670

<210> 12

<211> 3300

<212> DNA

<213> Artificial Sequence

<220>

<223> pYOFR1-2

<400> 12

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- <210> 13
- <211> 667
- <212> PRT
- <213> Artificial Sequence
- <220>
- <223> Light chain starts at residue 1 (D); Heavy chain starts at residue 215 (Q)
- <400> 13
- Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1 5 10 15
- Asp Arg Val Thr Ile Thr Cys Ser Ala Ser Gln Asp Ile Ser Asn Tyr 20 25 30
- Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Val Leu Ile 35 40 45
- Tyr Phe Thr Ser Ser Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly 50 55 60
- Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro 75 80
- Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Ser Thr Val Pro Trp 85 90 95
- Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala 100 105 110
- Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly 115 120 125
- Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala 130 135 140
- Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln 145 150 155 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Asp Phe Thr His Tyr Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Ala Asp Phe Lys Arg Arg Phe Thr Phe Ser Leu Asp Thr Ser Lys Ser Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Lys Tyr Pro Tyr Tyr Tyr Gly Thr Ser His Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr

Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly

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Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
660 665

<210> 14 <211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> HVR1 residues 26-35

<400> 14

Gly Tyr Thr Phe Thr Asn Tyr Gly Ile Asn 1 5 10

<210> 15

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> SGI consensus sequence

<400> 15

Gly Tyr Thr Phe Thr Ser Tyr Ala Ile Ser 1 5 10

<210> 16

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> SGII consensus sequence

<400> 16

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<210> 17

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> SGIII consensus sequence

<400> 17

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<210> 18
<211> 10
<212> PRT
<213> Artificial Sequence
<220>
<223> Y0317 VH HVR1 residues 26-35
<400> 18
Gly Tyr Asp Phe Thr His Tyr Gly Met Asn
<210> 19
<211> 11
<212> PRT
<213> Artificial Sequence
<220>
<223> E25 VH HVR1 residues 26-35
<400> 19
Gly Tyr Ser Ile Thr Ser Gly Tyr Ser Trp Asn
<210> 20
<211> 3300
<212> DNA
<213> Artificial Sequence
<220>
<223> E25 in pE25-11
<400> 20
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                                                                    120
agetttggag attategtea etgeaatget tegeaatatg gegeaaaatg accaacageg
                                                                    180
gttgattgat caggtagagg gggcgctgta cgaggtaaag cccgatgcca gcattcctga
                                                                    240
cgacgatacg gagctgctgc gcgattacgt aaagaagtta ttgaagcatc ctcgtcagta
                                                                    300
aaaagttaat cttttcaaca gctgtcataa agttgtcacg gccgagactt atagtcgctt
                                                                    360
tgtttttatt ttttaatgta tttgtaacta gtacgcaagt tcacgtaaaa agggtatcta
                                                                    420
gaattatgaa gaagaatatc gcatttette ttgcatetat gttcgttttt tetattgcta
                                                                    480
caaacgcgta cgctgatatc cagctgaccc agtccccgag ctccctgtcc gcctctgtgg
                                                                    540
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600 gcgatagggt caccatcacc tgccgtgcca gtcagagcgt cgattacgat ggtgatagct acatgaactg gtatcaacag aaaccaggaa aagctccgaa actactgatt tacgcggcct 660 720 cgtacctgga gtctggagtc ccttctcgct tctctggatc cggttctggg acggatttca 780 ctctgaccat cagcagtctg cagccggaag acttcgcaac ttattactgt cagcaaagtc acgaggatcc gtacacattt ggacagggta ccaaggtgga gatcaaacga actgtggctg 840 900 caccatctgt cttcatcttc ccgccatctg atgagcagtt gaaatctgga actgcctctg ttgtgtgcct gctgaataac ttctatccca gagaggccaa agtacagtgg aaggtggata 960 acgccctcca atcgggtaac tcccaggaga gtgtcacaga gcaggacagc aaggacagca 1020 cctacagcct cagcagcacc ctgacgctga gcaaagcaga ctacgagaaa cacaaagtct 1080 acgcctgcga agtcacccat cagggcctga gctcgcccgt cacaaagagc ttcaacaggg 1140 gagagtgtta attaaatcct ctacgccgga cgcatcgtgg cgagctcggt acccggggat 1200 1260 ctaggcctaa cgctcggttg ccgccgggcg ttttttattg ttgccgacgc gcatctcgaa tgaactgtgt gcgcaggtag aagctttgga gattatcgtc actgcaatgc ttcgcaatat 1320 1380 ggcgcaaaat gaccaacagc ggttgattga tcaggtagag ggggcgctgt acgaggtaaa gcccgatgcc agcattcctg acgacgatac ggagctgctg cgcgattacg taaagaagtt 1440 1500 attgaagcat cctcgtcagt aaaaagttaa tcttttcaac agctgtcata aagttgtcac 1560 ggccgagact tatagtcgct ttgtttttat tttttaatgt atttgtaact agtacgcaag ttcacgtaaa aagggtatct agaattatga agaagaatat cgcatttctt cttgcatcta 1620 tgttcgtttt ttctattgct acaaacgcgt acgctgaggt tcagctggtg gagtctggcg 1680 gtggcctggt gcagccaggg ggctcactcc gtttgtcctg tgcagtttct ggctactcca 1740 tcacctccgg atatagctgg aactggatcc gtcaggcccc gggtaagggc ctggaatggg 1800 ttgcatcgat tacgtatgac ggatcgacta actataaccc tagcgtcaag ggccgtatca 1860 ctataagtcg cgacgactcc aaaaacacat tctacctgca gatgaacagc ctgcgtgctg 1920 aggacactge egtetattat tgtgetegag geagecacta ttteggteac tggeaetteg 1980 ccgtgtgggg tcaaggaacc ctggtcaccg tctcctcggc ctccaccaag ggcccatcgg 2040 tettececet ggeacectee tecaagagea cetetggggg cacageggee etgggetgee 2100 tggtcaagga ctacttcccc gaaccggtga cggtgtcgtg gaactcaggc gccctgacca 2160 geggegtgea cacetteeeg getgteetae agteeteagg actetaetee eteageageg 2220 tggtgactgt gccctctagc agcttgggca cccagaccta catctgcaac gtgaatcaca 2280 agcccagcaa caccaaggtg gacaagaaag ttgagcccaa atcttgtgac aaaactcaca 2340

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<210> 21

<211> 669

<212> PRT

<213> Artificial Sequence

<220>

<223> Light chain starts at residue 1 (D); Heavy chain starts at residue 220 (E)

<400> 21

Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Asp Tyr Asp 20 25 30

Gly Asp Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro 35 40 45

Lys Leu Leu Ile Tyr Ala Ala Ser Tyr Leu Glu Ser Gly Val Pro Ser 50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser His Glu Asp Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Tyr Ser Ile Thr Ser Gly Tyr Ser Trp Asn Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Ser Ile Thr Tyr Asp Gly Ser Thr Asn Tyr Asn Pro Ser Val Lys Gly Arg Ile Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr Phe Tyr Leu Gln Met Asn Ser Leu

Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Gly Ser His Tyr Phe Gly His Trp His Phe Ala Val Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys 550 555 560 545 Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser 565 Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys 580 585 590 Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln 595 600 Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly 610 615 Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln 625 630 635 640 Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn 645 His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys 660 <210> 22 <211> 3300 <212> DNA Artificial Sequence <213> <220> E25 VH FR1 SGII in pE25-SGII <223> <400> gaattcaact tctccatact ttggataagg aaatacagac atgaaaaatc tcattgctga 60 gttgttattt aagcttgccc aaaaagaaga agagtcgaat gaactgtgtg cgcaggtaga 120 agetttggag attategtea etgeaatget tegeaatatg gegeaaaatg accaacageg 180 gttgattgat caggtagagg gggcgctgta cgaggtaaag cccgatgcca gcattcctga 240 cgacgatacg gagctgctgc gcgattacgt aaagaagtta ttgaagcatc ctcgtcagta 300 aaaagttaat cttttcaaca gctgtcataa agttgtcacg gccgagactt atagtcgctt 360 tgtttttatt ttttaatgta tttgtaacta gtacgcaagt tcacgtaaaa agggtatcta 420 gaattatgaa gaagaatatc gcatttcttc ttgcatctat gttcgttttt tctattgcta 480

540

600

caaacgcgta cgctgatatc cagctgaccc agtccccgag ctccctgtcc gcctctgtgg

gcgatagggt caccatcacc tgccgtgcca gtcagagcgt cgattacgat ggtgatagct

660 acatgaactg gtatcaacag aaaccaggaa aagctccgaa actactgatt tacgcggcct cgtacctgga gtctggagtc ccttctcgct tctctggatc cggttctggg acggatttca 720 780 ctctgaccat cagcagtctg cagccggaag acttcgcaac ttattactgt cagcaaagtc 840 acgaggatcc gtacacattt ggacagggta ccaaggtgga gatcaaacga actgtggctg caccatctgt cttcatcttc ccgccatctg atgagcagtt gaaatctgga actgcctctg 900 960 ttgtgtgcct gctgaataac ttctatccca gagaggccaa agtacagtgg aaggtggata 1020 acgccctcca atcgggtaac tcccaggaga gtgtcacaga gcaggacagc aaggacagca cctacagcct cagcagcacc ctgacgctga gcaaagcaga ctacgagaaa cacaaagtct 1080 acgcctgcga agtcacccat cagggcctga gctcgcccgt cacaaagagc ttcaacaggg 1140 gagagtgtta attaaatcct ctacgccgga cgcatcgtgg cgagctcggt acccggggat 1200 ctaggectaa egeteggttg eegeegggeg ttttttattg ttgeegaege geatetegaa 1260 1320 tgaactgtgt gcgcaggtag aagctttgga gattatcgtc actgcaatgc ttcgcaatat 1380. ggcgcaaaat gaccaacagc ggttgattga tcaggtagag ggggcgctgt acgaggtaaa 1440 gcccgatgcc agcattcctg acgacgatac ggagctgctg cgcgattacg taaagaagtt attgaagcat cctcgtcagt aaaaagttaa tcttttcaac agctgtcata aagttgtcac 1500 1560 ggccgagact tatagtcgct ttgtttttat tttttaatgt atttgtaact agtacgcaag 1620 ttcacgtaaa aagggtatct agaattatga agaagaatat cgcatttctt cttgcatcta 1680 tgttcgtttt ttctattgct acaaacgcgt acgctcaggt tcagctgcaa gagtctggcc 1740 egggeetggt gaaaccatet cagactetet cettgaettg taetgtttet ggetaeteca tcacctccgg atatagctgg aactggatcc gtcaggcccc gggtaagggc ctggaatggg 1800 1860 ttgcatcgat tacgtatgac ggatcgacta actataaccc tagcgtcaag ggccgtatca ctataagtcg cgacgactcc aaaaacacat tctacctgca gatgaacagc ctgcgtgctg 1920 1980 aggacactgc cgtctattat tgtgctcgag gcagccacta tttcggtcac tggcacttcg 2040 ccgtgtgggg tcaaggaacc ctggtcaccg tctcctcggc ctccaccaag ggcccatcgg tetteceect ggeaceetee tecaagagea cetetggggg cacageggee etgggetgee 2100 2160 tggtcaagga ctacttcccc gaaccggtga cggtgtcgtg gaactcaggc gccctgacca 2220 geggegtgea cacetteeeg getgteetae agteeteagg actetaetee eteageageg 2280 tggtgactgt gccctctagc agcttgggca cccagaccta catctgcaac gtgaatcaca ageccageaa caccaaggtg gacaagaaag ttgageccaa atettgtgac aaaactcaca 2340 catgcccacc gtgcccagca cctgaactcc tggggggacc gtcagtcttc ctcttccccc 2400

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Arg Phe Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser

<210> 23

<211> 669

<212> PRT

<213> Artificial Sequence

<220>

<223> Light chain starts at residue 1 (D); Heavy chain starts at residue 220 (Q)

<400> 23

Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Asp Tyr Asp
20 25 30

Gly Asp Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro 35 40 45

Lys Leu Leu Ile Tyr Ala Ala Ser Tyr Leu Glu Ser Gly Val Pro Ser 50 55 60

Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser His 85 90 95

65

Glu Asp Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105 110

Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
115 120 125

Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr 130 135 140

Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser 145 150 155 160

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr 165 170 175

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys 180 185 190

His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro 195 200 205

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys Gln Val Gln Leu Gln Glu 210 225 220

Ser Gly Pro Gly Leu Val Lys Pro Ser Gln Thr Leu Ser Leu Thr Cys 225 230 235 240

Thr Val Ser Gly Tyr Ser Ile Thr Ser Gly Tyr Ser Trp Asn Trp Ile 245 250 255

Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Ser Ile Thr Tyr 260 265 270

Asp Gly Ser Thr Asn Tyr Asn Pro Ser Val Lys Gly Arg Ile Thr Ile 275 280 285

Ser Arg Asp Asp Ser Lys Asn Thr Phe Tyr Leu Gln Met Asn Ser Leu 290 295 300

Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Gly Ser His Tyr

Phe Gly His Trp His Phe Ala Val Trp Gly Gln Gly Thr Leu Val Thr 325 330 335

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro 340 345 350

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala 370 375 380

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly 385 390 395

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly 405 410 415

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys 420 425 430

Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys 435 440 445

Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu 450 455 460

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu 465 470 475 480

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys 485 490 495

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys 500 505 510

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu 515 520 525

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys 530 535 540

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys

545 550 555 560

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser 565 570 575

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys 580 585 590

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln 595 600 605

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly 610 620

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln 625 630 635

Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn 645 650 655

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys 660 665

<210> 24

<211> 3300

<212> DNA

<213> Artificial Sequence

<220>

<223> pVG50

<400> 24

gaattcaact tctccatact ttggataagg aaatacagac atgaaaaatc tcattgctga 60 gttgttattt aagcttgccc aaaaagaaga agagtcgaat gaactgtgtg cgcaggtaga 120 agctttggag attatcgtca ctgcaatgct tcgcaatatg gcgcaaaatg accaacagcg 180 gttgattgat caggtagagg gggcgctgta cgaggtaaag cccgatgcca gcattcctga 240 cgacgatacg gagctgctgc gcgattacgt aaagaagtta ttgaagcatc ctcgtcagta 300 aaaagttaat cttttcaaca gctgtcataa agttgtcacg gccgagactt atagtcgctt 360 tgtttttatt ttttaatgta tttgtaacta gtacgcaagt tcacgtaaaa agggtatcta 420 gaattatgaa gaagaatatc gcatttcttc ttgcatctat gttcgttttt tctattgcta 480 caaacgcgta cgctgatatc cagatgaccc agtccccgag ctccctgtcc gcctctgtgg 540 gcgatagggt caccatcacc tgcagcgcaa gtcaggatat tagcaactat ttaaactggt 600

atcaacagaa accaggaaaa gctccgaaag tactgattta cttcacctcc tctctccact 660 ctggagtccc ttctcgcttc tctggatccg gttctgggac ggatttcact ctgaccatca 720 780 gcagtctgca gccagaagac ttcgcaactt attactgtca acagtatagc accgtgccgt 840 ggacgtttgg acagggtacc aaggtggaga tcaaacgaac tgtggctgca ccatctgtct tcatcttccc gccatctgat gagcagttga aatctggaac tgcttctgtt gtgtgcctgc 900 960 tgaataactt ctatcccaga gaggccaaag tacagtggaa ggtggataac gccctccaat cgggtaactc ccaggagagt gtcacagagc aggacagcaa ggacagcacc tacagcctca 1020 gcagcaccct gacgctgagc aaagcagact acgagaaaca caaagtctac gcctgcgaag 1080 tcacccatca gggcctgagc tcgcccgtca caaagagctt caacagggga gagtgttaat 1140 taaatcetet aegeeggaeg categtggeg ageteggtae eeggggatet aggeetaaeg 1200 cteggttgcc gccgggcgtt ttttattgtt gccgacgcgc atctcgaatg aactgtgtgc 1260 1320 gcaggtagaa gctttggaga ttatcgtcac tgcaatgctt cgcaatatgg cgcaaaatga 1380 ccaacagegg ttgattgatc aggtagaggg ggegetgtac gaggtaaagc cegatgecag cattectgae gaegataegg agetgetgeg egattaegta aagaagttat tgaageatee 1440 tegteagtaa aaagttaate tttteaacag etgteataaa gttgteaegg eegagaetta 1500 tagtcgcttt gtttttattt tttaatgtat ttgtaactag tacgcaagtt cacgtaaaaa 1560 gggtatctag aattatgaag aagaatatcg catttcttct tgcatctatg ttcgtttttt 1620 ctattgctac aaacgcgtac gctgaggttc agctggtgga gtctggcggt ggcctggtgc 1680 agccaggggg ctcactccgt ttgtcctgtg cagcttctgg ctataccttc accaactatg 1740 1800 gtatgaactg ggtccgtcag gccccgggta agggcctgga atgggttgga tggattaaca cctataccgg tgaaccgacc tatgctgcgg atttcaaacg tcgtttcact ttcagcttag 1860 1920 acacctccaa gtcgacagca tacctgcaga tgaacagcct gcgtgctgag gacactgccg 1980 tctattactg tgcaaagtac ccccactatt atgggagcag ccactggtat ttcgacgtct ggggtcaagg aaccetggtc accgtetect eggeetecac caagggeeca teggtettee 2040 ccctggcacc ctcctccaag agcacctctg ggggcacagc ggccctgggc tgcctggtca 2100 2160 aggactactt ccccgaaccg gtgacggtgt cgtggaactc aggcgccctg accagcggcg tgcacacett eceggetgte etacagteet caggacteta eteceteage agegtggtga 2220 ctgtgccctc tagcagcttg ggcacccaga cctacatctg caacgtgaat cacaagccca 2280 gcaacaccaa ggtggacaag aaagttgagc ccaaatcttg tgacaaaact cacacatgcc 2340 caccgtgccc agcacctgaa ctcctggggg gaccgtcagt cttcctcttc cccccaaaac 2400

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<210> 25

<211> 667

<212> PRT

<213> Artificial Sequence

<220>

<223> Light chain starts at residue 1 (D); Heavy chain starts at
residue 215 (E)

<400> 25

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly

1 10 15

Asp Arg Val Thr Ile Thr Cys Ser Ala Ser Gln Asp Ile Ser Asn Tyr 20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Val Leu Ile 35 40 45

Tyr Phe Thr Ser Ser Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly 50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro 65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Ser Thr Val Pro Trp 85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly 115 120 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala 130 135 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln 145 150 155 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser 165 170 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr 180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser 195 200 205

Phe Asn Arg Gly Glu Cys Glu Val Gln Leu Val Glu Ser Gly Gly Gly 210 215 220

Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly 225 230 235 240

Tyr Thr Phe Thr Asn Tyr Gly Met Asn Trp Val Arg Gln Ala Pro Gly 245 250 255

Lys Gly Leu Glu Trp Val Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro 260 265 270

Thr Tyr Ala Ala Asp Phe Lys Arg Arg Phe Thr Phe Ser Leu Asp Thr 275 280 285

Ser Lys Ser Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp 290 295 300

Thr Ala Val Tyr Tyr Cys Ala Lys Tyr Pro His Tyr Tyr Gly Ser Ser 305 310 315 320

His Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Leu Val Thr Val Ser 325 330 335

Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser 340 345 350

Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp 355 360 365

Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr 370 375 380

Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr 385 390 395 400

Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln 405 410 415

Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp 420 425 430

Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro 435 440 445

Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro 450 455 460

Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr 465 470 475 480

Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn 485 490 495

Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg
500 505 510

Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val 515 520 525

Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser 530 540

Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys 545 550 555 560

Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu 565 570 575

Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe 580 585 590

Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu
595 600 605

Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe 610 615 620

Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly 625 630 635

Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr 645 650 655

Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys 660 665

<210> 26

<211> 3300

<212> DNA

<213> Artificial Sequence

<220>

<223> pVKSGI with FR1-4 SGI consensus sequence

<400> 26

gaattcaact tctccatact ttggataagg aaatacagac atgaaaaatc tcattgctga 60 gttgttattt aagcttgccc aaaaagaaga agagtcgaat gaactgtgtg cgcaggtaga 120 agctttggag attatcgtca ctgcaatgct tcgcaatatg gcgcaaaatg accaacagcg 180 gttgattgat caggtagagg gggcgctgta cgaggtaaag cccgatgcca gcattcctga 240 cqacqatacq qaqctqctqc qcqattacqt aaaqaaqtta ttqaaqcatc ctcqtcaqta 300 aaaagttaat cttttcaaca gctgtcataa agttgtcacg gccgagactt atagtcgctt 360 tgtttttatt ttttaatgta tttgtaacta gtacgcaagt tcacgtaaaa agggtatcta 420 gaattatgaa gaagaatatc gcatttcttc ttgcatctat gttcgttttt tctattgcta 480 caaacgcgta cgctgatatc cagttgaccc agtccccgag ctccctgtcc gcctctgtgq 540 gcgatagggt caccatcacc tgcagcgcaa gtcaggatat tagcaactat ttaaactggt 600 atcaacagaa accaggaaaa gctccgaaag tactgattta cttcacctcc tctctccact 660

ctggagtccc ttctcgcttc tctggatccg gttctgggac ggatttcact ctgaccatca 720 780 gcagtctgca gccagaagac ttcgcaactt attactgtca acagtatagc accgtgccgt 840 ggacgtttgg acagggtacc aaggtggaga tcaaacgaac tgtggctgca ccatctgtct 900 tcatcttccc gccatctgat gagcagttga aatctggaac tgcttctgtt gtgtgcctgc 960 tgaataactt ctatcccaga gaggccaaag tacagtggaa ggtggataac gccctccaat 1020 cgggtaactc ccaggagagt gtcacagagc aggacagcaa ggacagcacc tacagcctca gcagcaccct gacgctgagc aaagcagact acgagaaaca caaagtctac gcctgcgaag 1080 tcacccatca gggcctgagc tcgcccgtca caaagagctt caacagggga gagtgttaat 1140 taaatcctct acgccggacg catcgtggcg agctcggtac ccgggggatct aggcctaacg 1200 cteggttgcc gccgggcgtt ttttattgtt gccgacgcgc atctcgaatg aactgtgtgc 1260 1320 gcaggtagaa gctttggaga ttatcgtcac tgcaatgctt cgcaatatgg cgcaaaatga 1380 ccaacagcgg ttgattgatc aggtagaggg ggcgctgtac gaggtaaagc ccgatgccag catteetgae gaegataegg agetgetgeg egattaegta aagaagttat tgaagcatee 1440 1500 tegteagtaa aaagttaate tttteaacag etgteataaa gttgteaegg eegagaetta 1560 tagtcgcttt gtttttattt tttaatgtat ttgtaactag tacgcaagtt cacgtaaaaa gggtatctag aattatgaag aagaatatcg catttcttct tgcatctatg ttcgtttttt 1620 ctattgctac aaacgcgtac gctcaggttc agctggtgca gtctggcgca gaggtgaaaa 1680 1740 agccaggggc ttcagttaaa gtatcctgta aagcttctgg ctataccttc accaactatg gtataaactg ggtccgtcag gccccgggtc agggcctgga atggatggga tggattaaca 1800 1860 cetatacegg tgaacegace tatgetgegg attteaaacg tegtgttact ateactgetg acacctccac tagcacagca tacatggaac tgtctagcct gcgctctgag gacactgccg 1920 tctattactg tgcacgttac ccgcactatt atgtgaacga gcggaagagc cactggtatt 1980 tegacgtetg gggteaagga accetggtea cegteteete ggeeteeace aagggeecat 2040 2100 eggtetteee eetggeacee teeteeaaga geacetetgg gggeacageg geeetggget gcctggtcaa ggactacttc cccgaaccgg tgacggtgtc gtggaactca ggcgccctga 2160 2220 ccagcggcgt gcacaccttc ccggctgtcc tacagtcctc aggactctac tccctcagca gegtggtgae tgtgecetet ageagettgg geacceagae etacatetge aaegtgaate 2280 acaagcccag caacaccaag gtggacaaga aagttgagcc caaatcttgt gacaaaactc 2340 acacatgccc accgtgccca gcacctgaac tcctgggggg accgtcagtc ttcctcttcc 2400 ccccaaaacc caaggacacc ctcatgatct cccggacccc tgaggtcaca tgcgtggtgg 2460

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<210> 27

<211> 670

<212> PRT

<213> Artificial Sequence

<220>

<223> Light chain starts at residue 1 (D); Heavy chain starts at
residue 215 (Q)

<400> 27

Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Ser Ala Ser Gln Asp Ile Ser Asn Tyr 20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Val Leu Ile 35 40 45

Tyr Phe Thr Ser Ser Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly 50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro 65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Ser Thr Val Pro Trp 85 Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala 100

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly 115 120 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala 130 135 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln 145 150 155 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser 165 170 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr 180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser 195 200 205

Phe Asn Arg Gly Glu Cys Gln Val Gln Leu Val Gln Ser Gly Ala Glu 210 215 220

Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly 225 230 235 240

Tyr Thr Phe Thr Asn Tyr Gly Ile Asn Trp Val Arg Gln Ala Pro Gly 245 250 255

Gln Gly Leu Glu Trp Met Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro 260 265 270

Thr Tyr Ala Ala Asp Phe Lys Arg Arg Val Thr Ile Thr Ala Asp Thr 275 280 285

Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp 290 295 300

Thr Ala Val Tyr Tyr Cys Ala Arg Tyr Pro His Tyr Tyr Val Asn Glu 305 310 315 320

Arg Lys Ser His Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Leu Val 325 330 335

Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala 340 345 350

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu 355 360 365

Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly 370 375 380

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser 385 390 395 400

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Leu 405 410 415

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr 420 425 430

Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr 435 440 445

Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe 450 455 460

Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro 465 470 475 480

Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val 485 490 495

Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr 500 505 510

Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val 515 520 525

Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys 530 535 540

Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser 545 550 555 560

Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro 565 570 575

Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val
580 585 590

Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly 595 600 605

Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp 610 620

Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp 625 630 635 640

Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His 645 650 655

Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys 660 665 670

<210> 28 <211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> VH FR2 SGIII

<400> 28

Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser 1 5 10

<210> 29

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> VH FR2 VNERK

<400> 29

Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Gly

<210> 30

<211> 32

<212> PRT

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<213> Artificial Sequence
<220>
<223> VH FR3 SGIII
<400> 30
Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln
Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg
                                25
<210> 31
<211> 32
<212> PRT
<213> Artificial Sequence
<220>
<223> VH FR3 VNERK
<400> 31
Arg Phe Thr Phe Ser Leu Asp Thr Ser Lys Ser Thr Ala Tyr Leu Gln
                                    10
Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Lys
           20
                               25
                                                   30
<210> 32
<211> 11
<212> PRT
<213> Artificial Sequence
<220>
<223> VH FR4 SGIII
<400> 32
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
<210> 33
<211> 32
<212> PRT
<213> Artificial Sequence
<220>
<223> VH FR3 SGI
<400> 33
Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Ser Thr Ala Tyr Leu Gln
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10

Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg 20 25 30